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Editorial

Zika Virus Epidemic in Rajasthan, India: Current Perspective

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Introduction

Zika, a flavivirus spread mainly by mosquitoes, belongs to the same genus as dengue and chikungunya. Some evidence that Zika has been in India for long comes from a 1954 survey, which found several Indians with Zika antibodies. However, this evidence wasn't conclusive, because other flaviviruses, like dengue, can also trigger Zika - neutralising antibodies. The first confirmed Indian case occurred in 2016 in Gujarat. Later, three more cases were detected, before the 2018 Rajasthan outbreak. Despite its long presence in Asia, Zika outbreaks in this region have been benign. This changed with a large French Polynesian outbreak in 2013 and a larger Brazilian one in 2015 [1].

First, Rajasthan's residents may not have been exposed to Zika before, and thus lack immunity. According to Nathan D. Grubaugh, a Zika genomics researcher at the Yale School of Public Health, American studies who that if 50-60% of a population is exposed to the virus, herd immunity develops and transmission stops. Another possibility is that mutations in the Rajasthan strain are helping it spread. More research is needed to identify such mutations [2]. The third explanation is that even though Zika has been around, it is being detected only now because we are looking. Until 2016, when Zika was declared a WHO global health emergency, Indian wasn't testing for Zika [3].

Pathogenesis

Zika virus is an icasohedral enveloped single standard positive sense RNA virus with approximately 11,000 nucleotides, which contains multiple copies of complex capsid protein. A single polyprotein containing 3423 amino acids is encoded to viral genome. By several viral and cellular proteases, the polyprotein is processed into three structural proteins, i.e., capsid, membrane and enveloped proteins [4]. These structural proteins are primarily responsible for formation of virus particles and has pivotal role in virus attachment, entry and encapsulation. It addition, it also involves in formation of seven non-structural (NS) proteins-NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5 which mediates viral genome replication polyprotein processing and counteraction of host innate antiviral response. Of all these NS protein NS1 has prominent role in viral replication. Zika virus has a 3 non coding region with conserved sequences organized in a CS1-CS2-CS3 pattern. This is new for the Spondweni virus group [5]. Kedougou and Bagaza viruses have also been sequenced with Genbank accession numbers AY632540 and AY632545 respectively. Based on the partial sequence of NS5 protein, Bagaza virus in 98% identical to Israel Turkey virus (ITV) Genbank EU303198, both viruses show a high degree of immune (neutralization similarity) [6]. For rapid detection and identification of Flavivirus was developed using a set of universal oligonucleotide primers through a reverse transcriptase (RT-PCR) protocol. Among the mosquito borne Flaviviruses the highly conserved virus corresponds to sequences in the 3-non coding region and in the NS5 gene. A less numbers of nucleotide were investigated from the C-terminus of NS5 gene (i.e., about 291-297 nucleotides showed 56-76 similarities when compared to the 3-non coding region which is having more number of nucleotides (i.e., 193-42 nucleotides) showed only 26-36% similarity. Nucleic acid hybridization test was used to detect the recombinant plasmids containing the Flavivirus sequences, from the RT-PCR products derived from the virus RNA which were extracted from experimental mosquitoes. In 2010 the virus was isolated through gel purification technique in Cambodia. It is then subjected to PCR; it has produced a 100 bp fragment with 100% sequence identity to GenBank accession number EU545988 to Zika virus with nucleic acid position 8,969 of NS5 gene by Haem agglutination-inhibition tests [7].

It is difficult to confirm Zika infection (out of acute phase of 4-5 days) by serology, due to a very high cross-reactivity with DENV. In such a situation, performing serology is not advised where high false positivity will create panic. At present, only a few commercial serology kits are available. It is difficult to ascertain whether there will be congenital disabilities in children born to ZIKV-infected women or with history of infection. It is so far not feasible to screen all asymptomatic pregnant women by molecular tests [8]. Now, that the presence of ZIKV in the country is confirmed, microcephaly may be made a notifiable disease in the country so as to indirectly estimate the burden caused by ZIKV Research is required to understand the ZIKV natural cycle in India and several questions need to be addressed *viz.*, (i) how is the virus maintained in nature (vector biology)?, (ii) what is the threshold titre of ZIKV for mosquito population in India?, (iii) the population genetic studies on different vector populations with reference to the ZIKV susceptibility/refractivity need to be done, (iv) what is the spectrum of pregnancy outcome in ZIKV infected pregnant females?, (v) are there any other vertebrate hosts prevalent in India?, and (vi) what is the effect of interaction of other flaviviruses on ZIKV transmission? The virus has lived a ubiquitous life for decades in tropical and equatorial zone and has also not shown any dramatic evolutionary mutations, but the vector biology and pathogenesis of the ZIKV need to be better understood.

It will be ideal to make Zika and microcephaly screening mandatory amongst pregnant women and initiate surveillance network in collaboration with hospitals and laboratories across the country, which will help us know the burden of ZIKV in India. The four ZIKV cases are only 'tip of the iceberg' and many subclinical cases may be present; hence, an efficient surveillance network needs to be initiated, but in a country like India, such ventures are cost-intensive and require political commitment [9].

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Conclusion

It is not clear if the person (index case) or others who had contracted the infection had travelled to any country where there is a Zika infection risk. The absence of travel history outside India in the virus is prevalent in the mosquito population. Spread through sex, without multiple instances of infection by mosquitoes is unlikely, given the spurt in the number of cases within a narrow time window in a small community. Since Zika infection during pregnancy can cause severe birth defects, particularly microcephaly (small size of the head), all the 22 pregnant women infected must be monitored. Also, as there is no cure for microcephaly at birth, there should be campaigns to educate people living in the outbreak area to avoid sex, particularly with the internet of getting pregnant, till the outbreak is under control. The long winter ahead monsoon in the eastern onset of the northeast monsoon in the eastern coast on Indian is conductive for the mosquito to multiply and spread. This calls for a high level of alert [8].

The environment in India is conducive for ZIKV because of preponderance of the *Ae. Aegypti* mosquitoes. Though these mosquitoes breed throughout the year in and around the houses in potable water sources, the density is extremely high during monsoon since more number of breeding sites becomes available. High humidity and optimal temperature support their survival for many days; thus, they get opportunity to lay eggs every 3-4 days and have multiple blood meals. The most effective and long-term preventive and control measure for *Ae.aegypti* as recommended by the authorities is 'source reduction involving community participation' [10].

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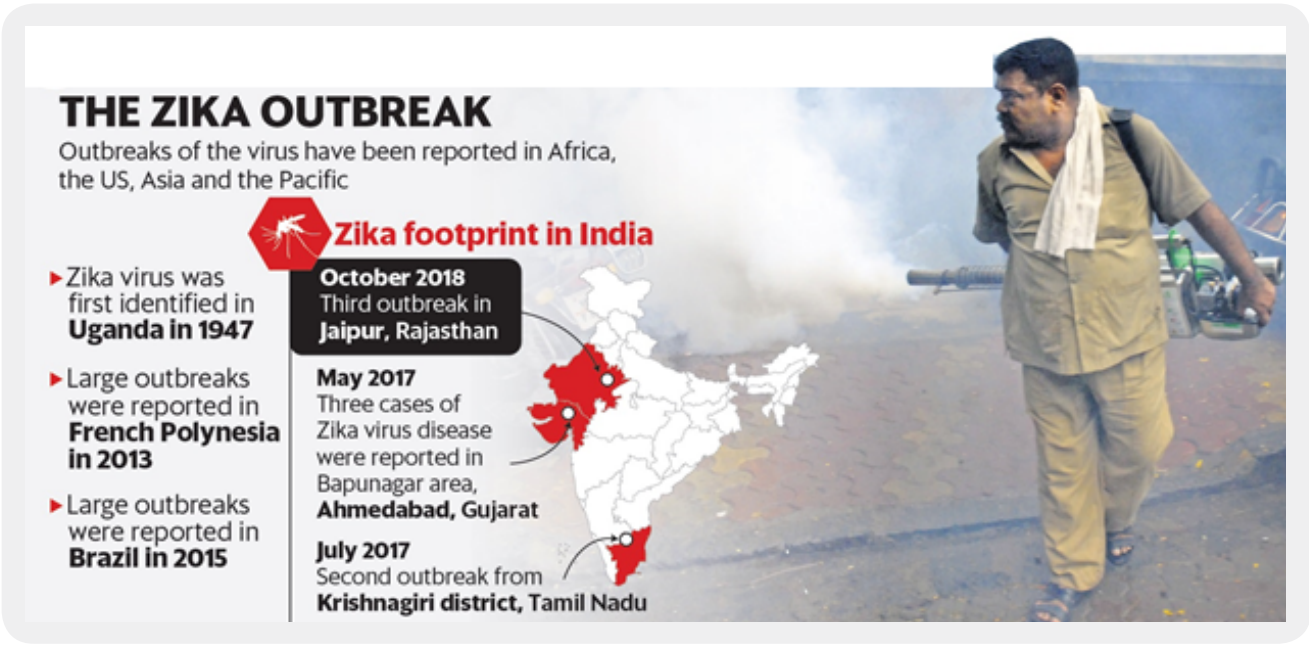
Conflict of Interest

Nil



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